

Lipoproteins



Assistant prof Dr : **Amer Mohamed**

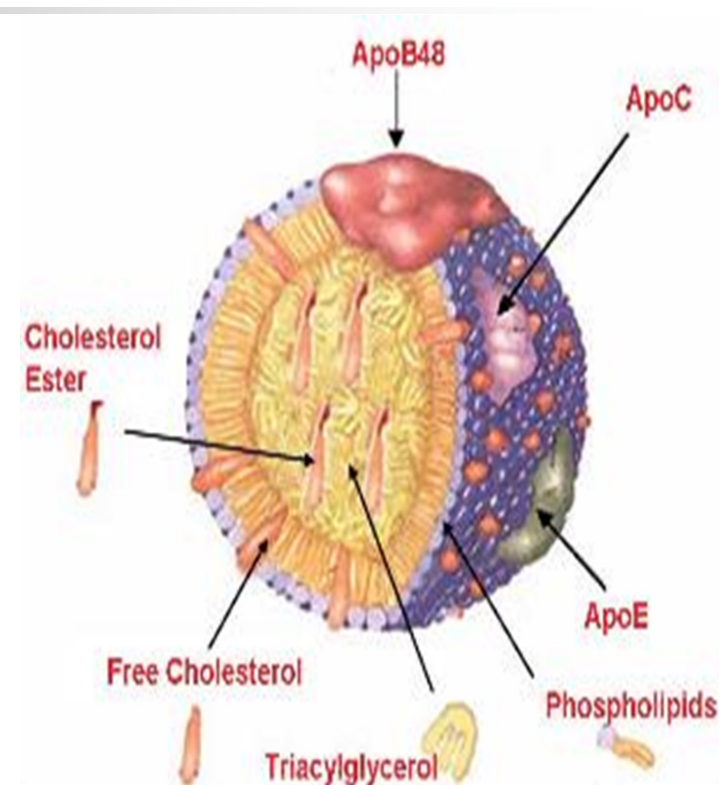


Objectives

- Define lipoproteins and explain the rationale of their formation in blood.
- List different types of plasma lipoproteins and describe their composition and features.
- Explain the metabolism of individual lipoproteins.

Introductions

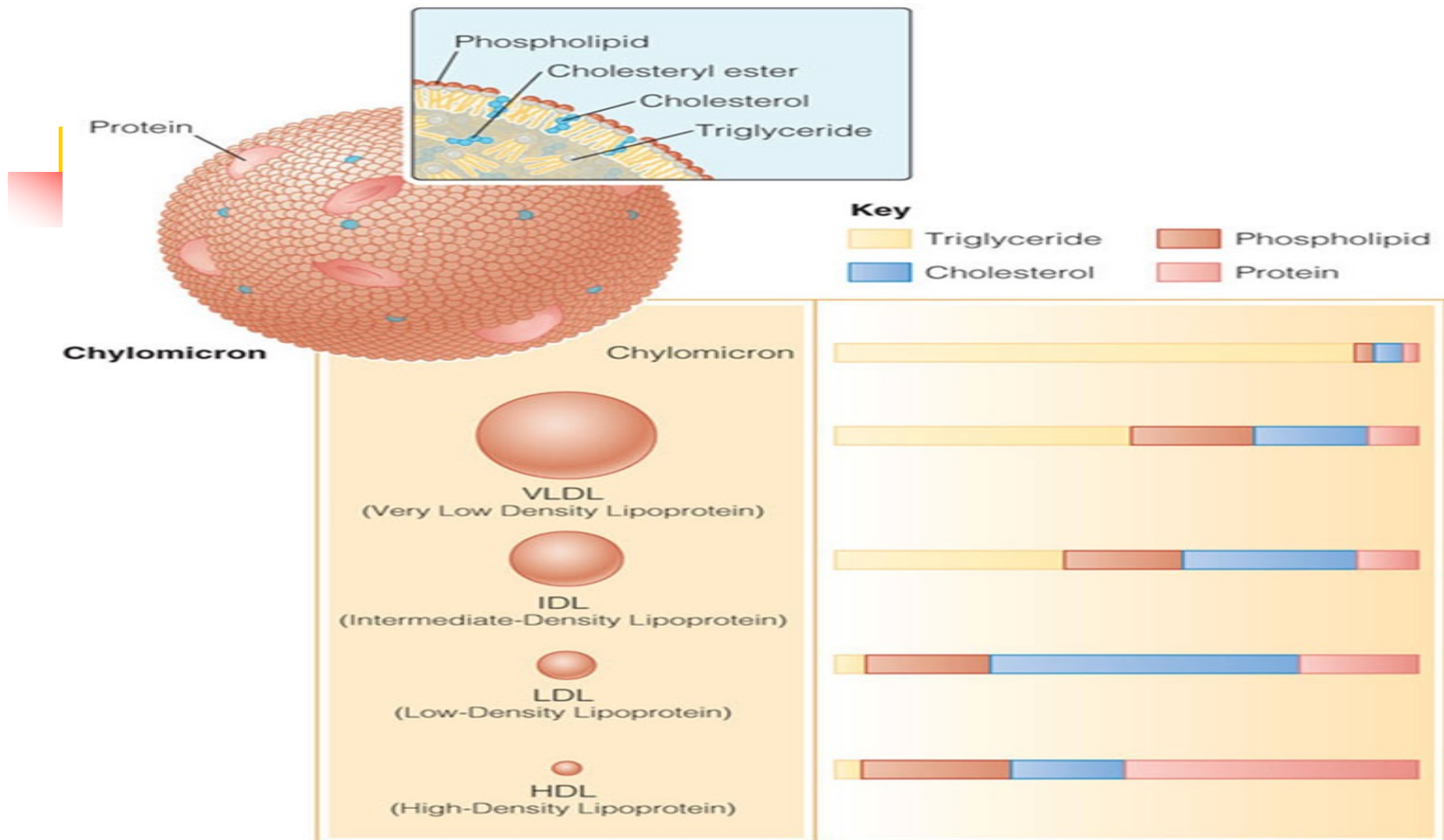
- Lipoproteins structure :
 - Core of TAG and CE
 - Surface of PL and some Chol.
 - Apolipoproteins or Apoproteins:
ApoB , ApoC & ApoE
- Lipid transported by :
 - Lipoproteins
 - Albumin-**FFA**





Lipoproteins

- Lipids associated with proteins that serve as transporter for them in blood
- Plasma lipids & apolipoproteins exists in dynamic state
- Distinguished from each other by **size** , **density** & **composition**
- Each contains different **types & amounts** of **lipids** & **proteins**
 - The more lipid, the lower the density
 - The more protein, the higher the density





Lipoproteins

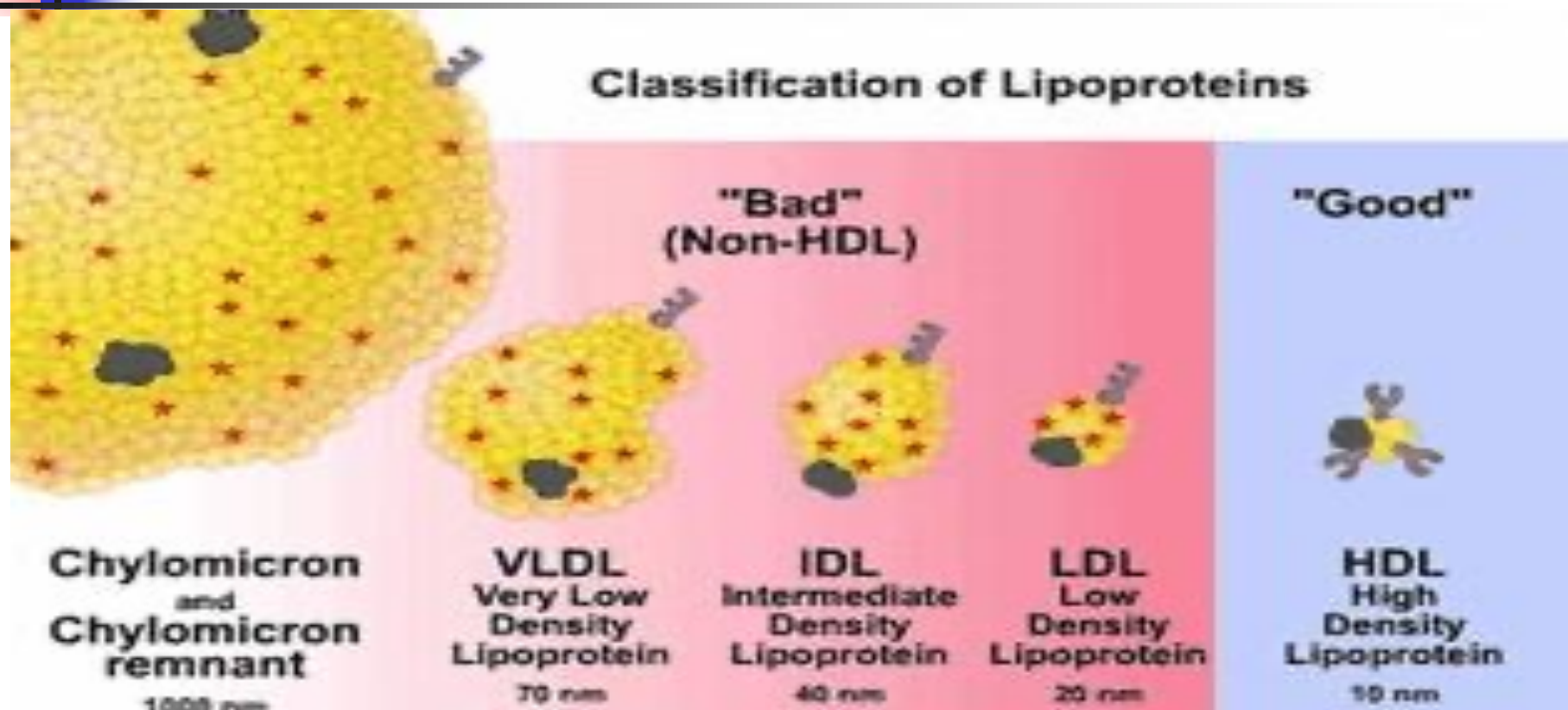
- Lipoproteins formed from lipid fraction & protein one that called **apolipoproteins or apoproteins**:
 - **APOPROTEINS** :
 - Globulins synthesized by liver (mainly) & intestine
 - Function:
 - **Transport** lipids in blood , as **lipoproteins**
 - Providing **recognition** sites for cell-surface receptors
 - Acts as **activators** or **coenzymes** for some enzymes involved in lipoprotein metabolism
 - Divided into five major classes : A , B,C,D,E
 - Most classes having subclasses, e.g, apo A-I & apo C-II,..
 - **LIPID FRACTION INCLUDES** :
 - Triacylglycerol (TAG), Cholesterol (CE) , Phospholipids (PL) Free fatty acids (FFA)



Lipoproteins ,types

- Chylomicrons
- VLDL – Very low density lipoprotein
- IDL – Intermediate density lipoprotein
- LDL – Low density lipoprotein
- HDL – High density lipoprotein
 - Origin
 - Lipids
 - Proteins
 - Functions
 - Catabolism

Lipoproteins ,types

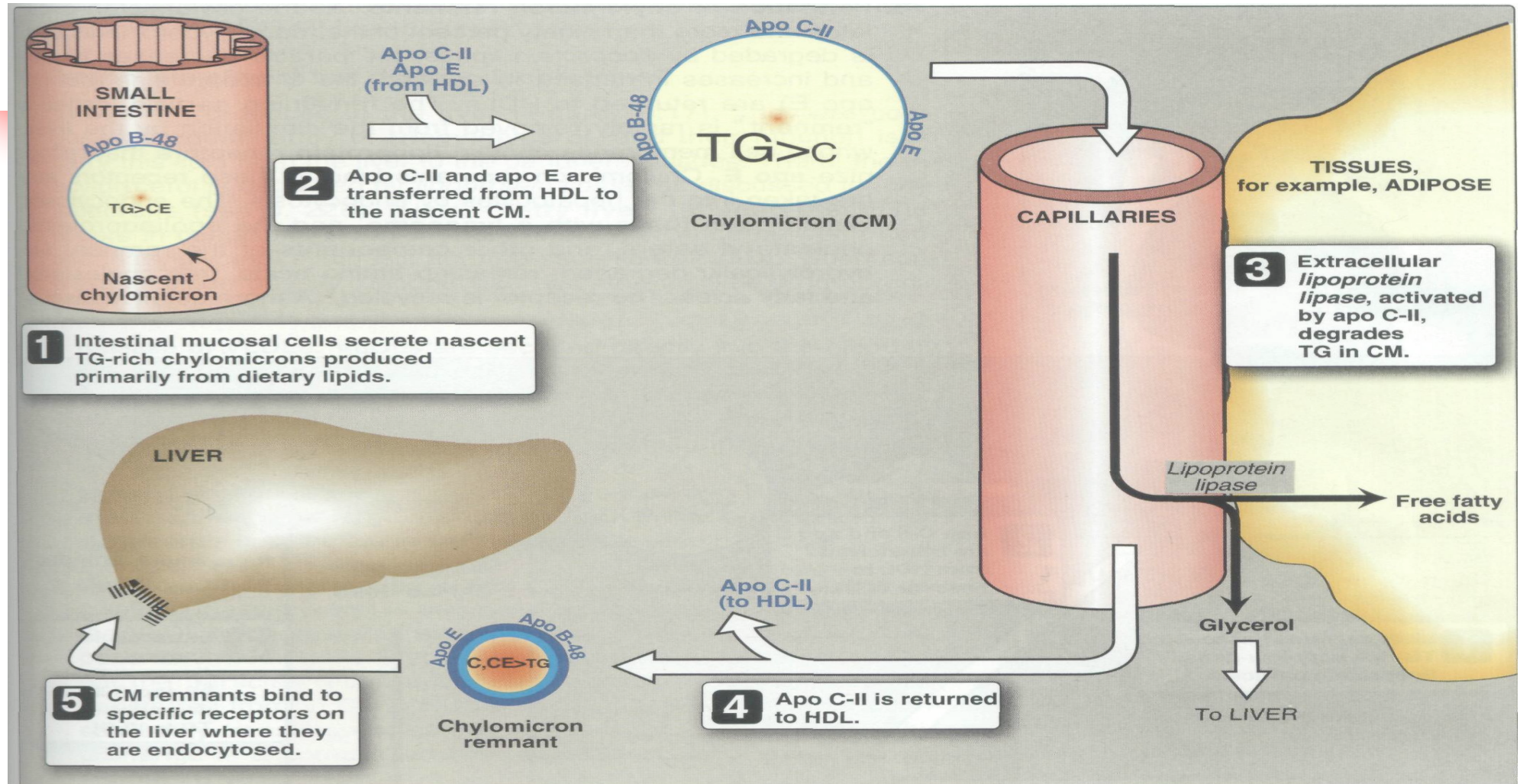




Chylomicrons

- Made by intestinal mucosal cells
- Lipid, most (Dietary = Exogenous) TAG (mainly), PL , CE , FFA
- Protein, little (1-2%)
 - Apo B- 48.
 - Receives Apo E , Apo C (mainly C-II) from HDL
- By lipoprotein lipase & in presence of Apo C-II ; TAG gives FFA (to muscles for energy or stored in adipose tissues) & glycerol (go to liver for lipogenesis or gluconeogenesis or glycolysis ,...)
- **Chylomicron remnants**: Lipoprotein particle that remains after a chylomicron has lost most of its fatty acids (loss more than 90% of its TAG):
 - Taken up by liver
 - Contents reused or recycled

Chylomicrons metabolism



The metabolism of chylomicrons:

1- Nascent chylomicrons: synthesized in intestinal cells to carry the absorbed dietary lipids to liver and other tissues.

They are formed by the following steps:

a- **Lipid:** synthesized in the smooth endoplasmic reticulum (SER).

b- **Apolipoproteins:** synthesized in the ribosomes on the rough endoplasmic reticulum (RER).

- ApoB-100 represents 100% expression of apoB gene, while Apo B-48 represents 48% expression of apoB gene.
- ApoB-48 forms 48% of the apoB-100.

c- **Assembly of both lipids and proteins** then packaged in secretory vesicles and released to intercellular space by exocytosis as **nascent chylomicrons** which drained by the intestinal lacteals to the thoracic duct then to blood stream

2- Mature chylomicrons: occurs by receiving apo C II and apo E from HDL

3- Degradation by plasma lipoprotein lipase enzyme:

This enzyme is attached to a proteoglycan termed heparan sulfate on the endothelial lining of the capillary walls of many tissues e.g. adipose tissue.....

Lipoprotein lipase is termed the **clearing factor** as it produces clearance of the turbidity produced by chylomicrons in plasma.

The enzyme **catalyzes** hydrolysis of triacylglycerols present in both lipoproteins into glycerol and free fatty acids. This action is **activated** by **apo C-II**

Glycerol is taken by liver cells mainly. **Free fatty acids** either enter within the tissues or transported bound to plasma albumin for uptake and metabolism by liver cells.

4- Chylomicron remnants: occurs by **hydrolysis** of TAG by the lipoprotein lipase and **transferration** of apo CII to HDL.

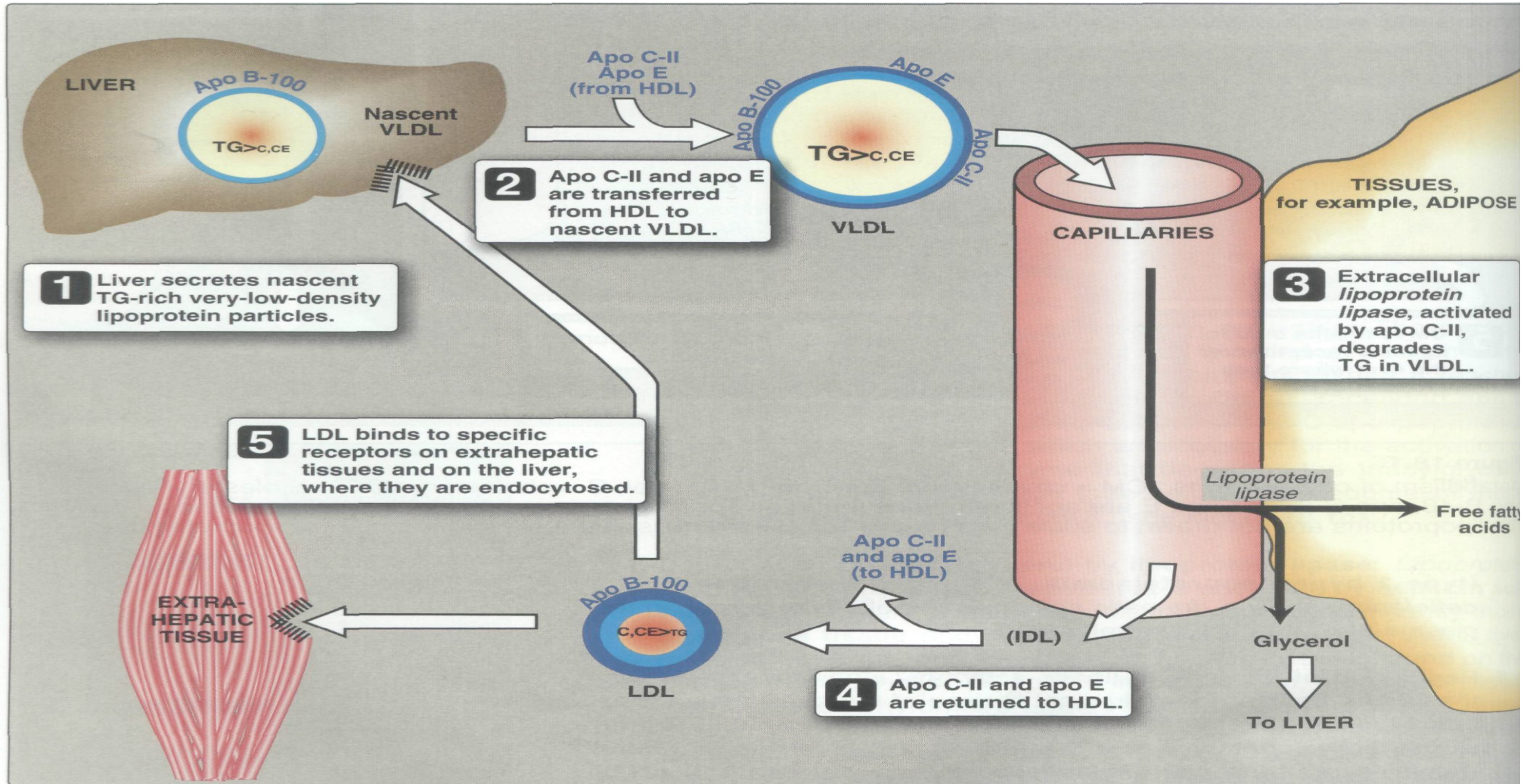
- The remaining particles are termed **chylomicron remnants**.
- They **have less percent** of TAG and **higher percent** of cholesterol, cholesteryl esters and phospholipids.
- Also TAG is transferred to HDL in exchange with cholesteryl esters, this is catalyzed by **cholesteryl ester transfer protein** (CETP or termed apo D).
- The remnants are **endocytosed** by liver cells through specific receptors for apo E.
- In liver cells, the different components are hydrolyzed and metabolized or reused for synthesis of lipoproteins.



Very Low Density Lipoproteins

- Made by liver
- Lipid, most (Endogenous) TAG (mainly), little PL , CE
- Protein, (7-10 %)
 - Apo B-100
 - Receives Apo E , Apo C (mainly C-II) from HDL
- More dense than chylomicrons
- Delivers (Endogenous) lipids (mainly TAG) to cells
- Also transfers TG & PL to HDL in exchange with CE esters by cholesterol ester transfer protein

VLDL metabolism



The metabolism of VLDL is summarized as follows:

1. Synthesis of **nascent VLDL** by liver cells:

Nascent VLDL are formed by liver cells and contain a specific protein termed apo B-100.

2. Conversion to **mature VLDL**:

Nascent VLDL are released from liver cells into blood, where they receive apo C and apo E from HDL to form the mature VLDL.

3. **Degradation** by plasma **lipoprotein lipase** enzyme:

As in chylomicrons, this enzyme catalyzes hydrolysis of the TAG into glycerol and free fatty acids.

4. Formation of **VLDL remnants (IDL)**:

They are also termed intermediate density lipoproteins (IDL). They are formed after the action of lipoprotein lipase and removal of apo C that returns back to HDL.

5. **Conversion of IDL to LDL**:

This is achieved by further hydrolysis of TAG, and removal of apo E (it returns back to HDL).

Also TAG is transferred to HDL in exchange with cholesteryl esters, this is catalyzed by cholesteryl ester transfer protein (apo D).



Intermediate Density Lipoproteins

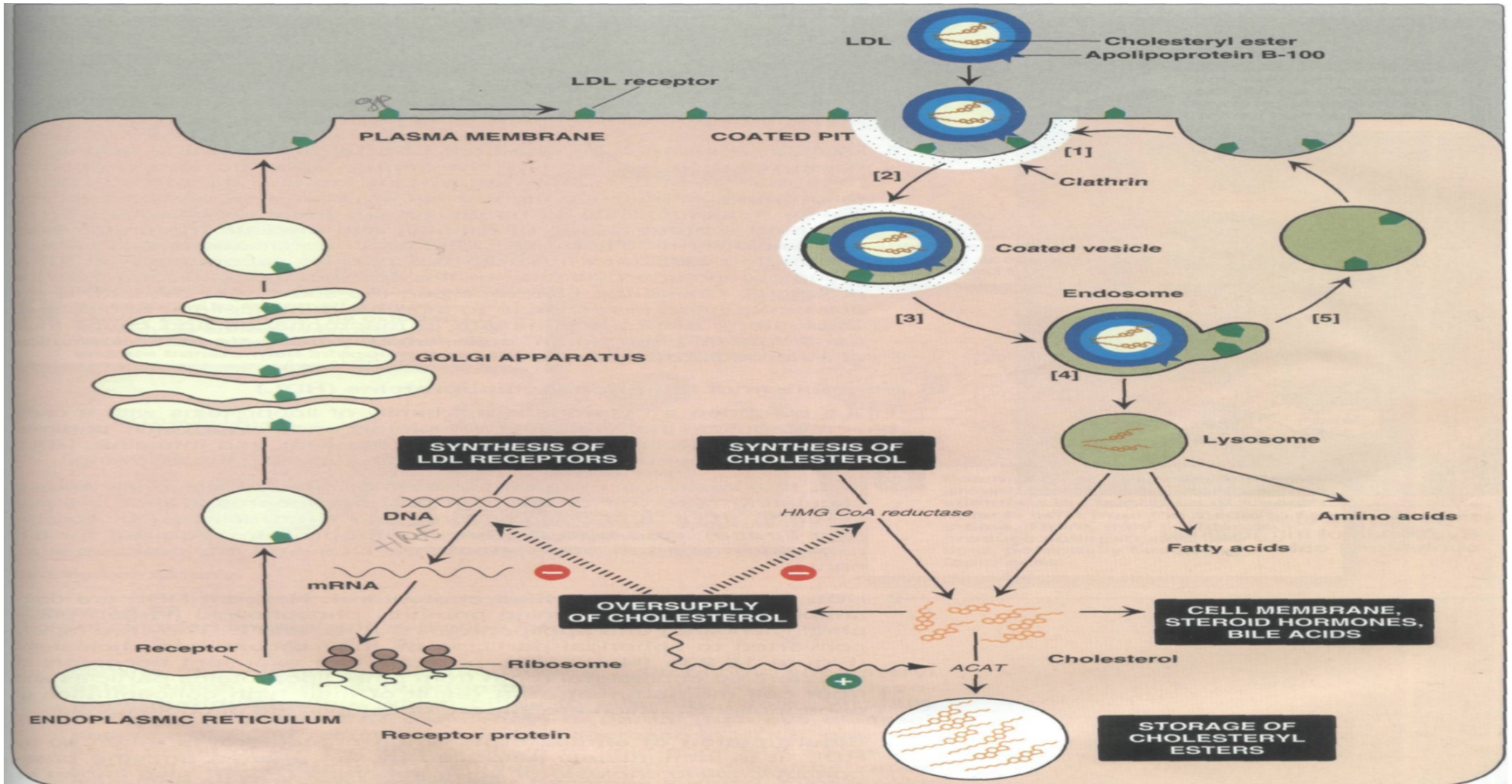
- Lipoprotein that results from loss of TAG & PL from VLDL
- Major lipid is cholesterol esters
- Proteins similar to VLDL but greater percentage (15%)
 - ApoB-100, Apo C, Apo E
- Taken up by liver or remain in circulation
- Converted to low-density lipoproteins (LDL) after giving its Apo C & also Apo E to HDL

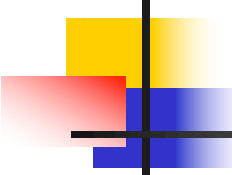


Low-Density Lipoproteins

- Made in circulation from VLDL
- Lipid , (mainly cholesterol) , PL
- Protein (21%)
 - Apo B-100
 - Binds to specific LDL receptor
- LDL receptors
 - Membrane-bound proteins that bind LDL, causing them to be taken up & dismantled
- Delivers cholesterol from liver to cells.

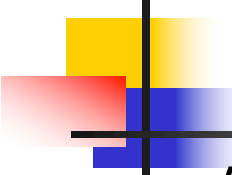
VLDL metabolism





High Density Lipoproteins

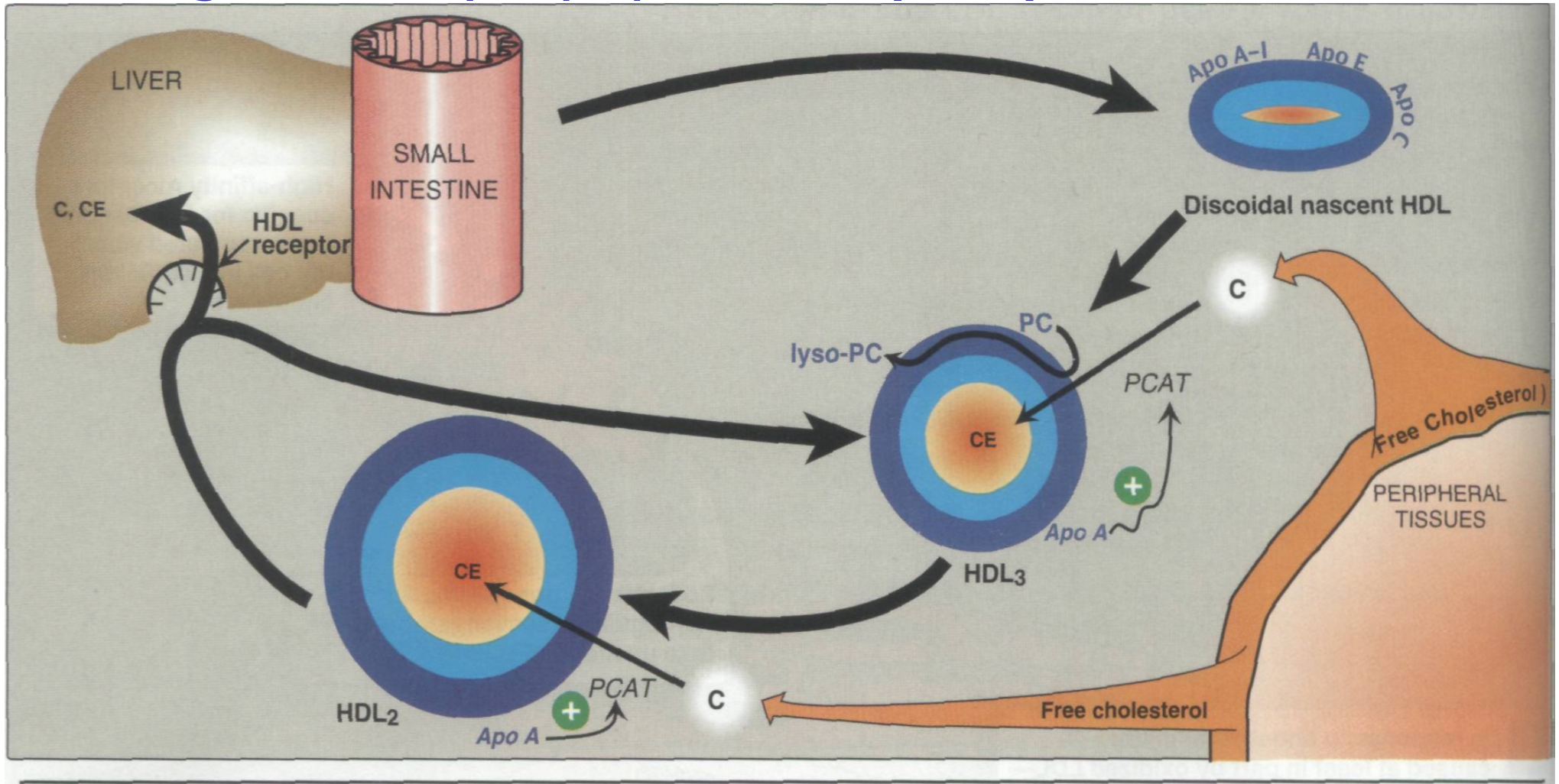
- Made by liver , intestine !
- Protein (50%)
 - Apo A-I & A-II , Apo C, Apo E
- Lipid , mainly PL then CE then TAG
- Lowest lipid-to-protein ratio



High Density Lipoproteins

- A reservoir of apoproteins: Apo C , Apo E , Apo A
- Reverse cholesterol transport
 - Circulates in blood to collect excess cholesterol from cells & esterifying it by LCAT (which activated by Apo A-I)
 - Transported it back to liver for excretion or transport again to circulation
 - Or to steroidogenic cells for hormone synthesis

High Density Lipoproteins (HDL)



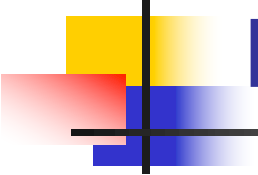
Important of spherical HDL:

- Act as **reservoir** for different apoproteins (C&E), which are important for metabolism of chylomicrons and VLDL.
- **Removal of free cholesterol** from the extrahepatic tissues and esterified by LCAT forming cholesterol esters. (**reverse cholesterol transport**)
- HDL provide cholesteryl esters to:
 - Chylomicron remnants and LDL in exchange with triacylglycerols by the mean of CETP (apo D) .
 - Liver where cholesteryl esters are hydrolyzed. The free cholesterol released is either:
 - 1- Repacked into lipoproteins
 - 2- Converted to bile acids
 - 3- Secreted in bile.



Lipoproteins & CVD risk

- High levels of HDL-cholesterol **decrease** the risk of atherosclerosis
- High levels of LDL-cholesterol **increase** the risk of atherosclerosis
- **Role of Lipoprotein (a) in heart disease:**
 - Structure : 1 mol of LDL + 1 mol of Apoprotein (a)
 - Apo (a) is highly homologous to **plasminogen** (precursor of blood protease which producing fibrinolysis). So, Apo (a) competes with it preventing its fibrinolysis action.
 - Diet containing **trans-fatty acids** **increasing** LDL and Lp(a) **Estrogen** **decreasing** LDL and Lp(a).
 - Familial Lp(a) excess : leading to premature coronary heart disease atherosclerosis and thrombosis.



Recommended blood lipids

- Total cholesterol : <200 mg/dL
- Triglycerides : <200 mg/dL
- LDL-cholesterol : <130 mg/dL
- HDL-cholesterol : >35 mg/dL